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Osteogenic activity of the fourteen types of human bone morphogenetic proteins (BMPs).

Cheng H, Jiang W, Phillips FM, Haydon RC, Peng Y, Zhou L, Luu HH, An N, Breyer B, Vanichakarn P, Szatkowski JP, Park JY, He TC.

Department of Surgery, The University of Chicago Medical Center, Illinois, USA. tche@surgery.bsd.uchicago.edu

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BACKGROUND: Bone morphogenic proteins (BMPs) are known to promote osteogenesis, and clinical trials are currently underway to evaluate the ability of certain BMPs to promote fracture-healing and spinal fusion. The optimal BMPs to be used in different clinical applications have not been elucidated, and a comprehensive evaluation of the relative osteogenic activity of different BMPs is lacking. METHODS: To identify the BMPs that may possess the most osteoinductive activity, we analyzed the osteogenic activity of BMPs in mesenchymal progenitor and osteoblastic cells. Recombinant adenoviruses expressing fourteen human BMPs (BMP-2 to BMP-15) were constructed to infect pluripotent mesenchymal progenitor C3H10T1/2 cells, preosteoblastic C2C12 cells, and osteoblastic TE-85 cells. Osteogenic activity was determined by measuring the induction of alkaline phosphatase, osteocalcin, and matrix mineralization upon BMP stimulation. RESULTS: BMP-2, 6, and 9 significantly induced alkaline phosphatase activity in pluripotential C3H10T1/2 cells, while BMP-2, 4, 6, 7, and 9 significantly induced alkaline phosphatase activity in preosteoblastic C2C12 cells. In TE-85 osteoblastic cells, most BMPs (except BMP-3 and 12) were able to induce alkaline phosphatase activity. The results of alkaline phosphatase histochemical staining assays were consistent with those of alkaline phosphatase colorimetric assays. Furthermore, BMP-2, 6, and 9 (as well as BMP-4 and, to a lesser extent, BMP-7) significantly induced osteocalcin expression in C3H10T1/2 cells. In C2C12 cells, osteocalcin expression was strongly induced by BMP-2, 4, 6, 7, and 9. Mineralized nodules were readily detected in C3H10T1/2 cells infected with BMP-2, 6, and 9 (and, to a lesser extent, those infected with BMP-4 and 7). CONCLUSIONS: A comprehensive analysis of the osteogenic activity of fourteen types of BMPs in osteoblastic progenitor cells was conducted. Our results suggest an osteogenic hierarchical model in which BMP-2, 6, and 9 may play an important role in inducing osteoblast differentiation of mesenchymal stem cells. In contrast, most BMPs are able to stimulate osteogenesis in mature osteoblasts.

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